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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

ZAREK, PAUL E

ART UNIT

PAPER NUMBER

1617

MAIL DATE

DELIVERY MODE

04/02/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/557,922	Applicant(s) MORI ET AL.	
	Examiner Paul Zarek	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5 and 7-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. Claim 1 has been amended and Claims 4 and 6 have been cancelled by the Applicant in correspondence filed on 01/28/2009. Claims 1-3, 5, and 7-14 are currently pending. This is the second Office Action on the merits of the claim(s).

RESPONSE TO ARGUMENTS

2. Claims 1 and 4 were rejected under 35 U.S.C. 102(b) as being anticipated by Hattori (US Patent No. 6,268,395, provided in IDS). This rejection is moot in light of the amendment to Claim 1 and the cancellation of Claim 4.

3. Claims 2, 3, and 5 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hattori (above). Applicants traversed this rejection on the grounds that Hattori teaches neither the presence of a protecting group on R₁, nor that esters, alkyl groups or ethers are known to be protecting groups. Applicants assert that the disclosure of Hattori suggests that differences within the phorbol derivative taught therein may affect its tumor promoting, antitumor and anti-HIV-1 effects (col 3, lines 58-63). Applicants assert that Hattori, therefore, teaches that altering the phorbol derivative taught by Hattori “will alter the effectiveness of the overall molecules as anti-HIV agents” (Reply, pg 8, line 7, emphasis added). Examiner respectfully disagrees.

4. Hattori teaches numerous compounds, some of which indicate R¹ as an ester (Table 2). Many of the compounds with R₁ as an ester have a specific safety index at or above 10 (Table 3; Please see previous Office Action, pg 4, lines 2-6 for methodology of converting Hattori safety

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index calculation to that disclosed in the instant application). That some phorbol ester derivatives may have different faculties than those disclosed in Hattori does not necessarily mean that all differing phorbol derivatives would be ineffective against HIV-1. Because esters, alkyl groups, and ethers (including thioesters and thioethers) are all known protecting groups (See Carey and Sundberg, Advanced Organic Chemistry, 3rd ed., 1990, Section 13.1.1; and Greene and Wuts, Protective Groups in Organic Synthesis, 2nd ed., 1991, Chapter 2), one of ordinary skill in the art would reasonably expect, in the absence of unexpected results, that altering R₁ of Hattori would result in a phorbol derivative with a retained, or even enhanced, anti-HIV-1 capacity. Therefore, thioesters, ethers, thioethers, and alkyl groups are *prima facie* obvious variants of the phorbol derivatives disclosed by Hattori. Thus, the rejection of Claims 2, 3, and 5 over Hattori is maintained.

5. Claims 7-14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hattori (above) as applied to Claims 1 and 4 above and in further view of Raffanti and Haas (Goodman & Gilman's The Pharmaceutical Basis of Therapeutics, 2001). Applicants traversed this rejection on the grounds that Hattori does not teach or render obvious the phorbol derivatives of Claims 1. Examiner respectfully disagrees for the reasons discussed above. Applicants have not disagreed with application of Raffanti and Haas with respect to the motivation to combine the claimed phorbol derivative with another anti-HIV drug. Therefore, the rejection of Claims 7-14 over Hattori (above) in view of Raffanti and Haas is maintained.

Amended Claim 1 is examined on their merits and the following **FINAL** rejection is made.

Claim Rejections - 35 USC § 103

6. The text Title 35, U.S.C § 103 can be found in a prior Office action.
7. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hattori (above).
8. Claim 1 is drawn to an antiviral preparation comprising formula 1, and was amended such that R₁ can no longer be CO(CH₂)_eCH₃.
9. Hattori teaches an phorbol-derivative anti-HIV composition wherein R₁ is – CO(CH₂)_eCH₃, where e is 0, R₂ is -CO(CH₂)_nCH₃, wherein n is 8, and R₃, R₄, and R₅ are –H (compound 6). Compound 6 was assayed in MT-4. It possessed an IC₁₀₀ (the concentration to fully inhibit the cytopathic effect) of 0.0076 µg/mL, and a CC₀ (minimum cytotoxic concentration) of 62.5 µg/mL. This would yield a calculated CC₅₀/EC₅₀ of 32,895, which meets the safety index limitation of Claim 1. Hattori does not teach a phorbol derivative wherein R₁ is other than CO(CH₂)_eCH₃. However, as discussed above, esters, alkyl groups, and ethers (including thioesters and thioethers) are all known protecting groups, and one of ordinary skill in the art would reasonably expect that altering R₁ of Hattori would result in a phorbol derivative with a retained, or even enhanced, anti-HIV-1 capacity. Therefore, thioesters, ethers, thioethers, and alkyl groups are *prima facie* obvious variants of the phorbol derivatives disclosed by Hattori.

Conclusion

10. Claims 1-3, 5, and 7-14 are rejected.

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11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

12. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Rita J. Desai/
Primary Examiner, Art Unit 1625